WEST Search History

DATE: Tuesday, September 16, 2003

Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT,PGPB,EPAB,DWPI,TDBD; THES=ASSIGNEE; PLUR=YES; OP=ADJ		
L6	screen$ and (XRCC4 and (DNA adj ligase adj IV) and DNA adj PKcs and phosphorylat$)	5	L6
L5	screen$ and (XRCC4 same (DNA adj ligase adj IV) same DNA adj PKcs same phosphorylat$)	0	L5
L4	screen$ and (XRCC4 same (DNA adj ligase adj IV) and DNA adj PKas and phosphorylat$)	0	L4
L3	screen$ and (XRCC4 same (DNA adj ligase adj IV) same DNA adj PKas same phosphorylat$)	0	L3
L2	screen$ same XRCC4 same (DNA adj ligase adj IV) and DNA adj PKas and phosphorylat$	0	L2
L1	screen$ same XRCC$ same (DNA adj ligase adj IV) same DNA adj PKas and phosphorylat$	0	L1

END OF SEARCH HISTORY

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Search Results - Record(s) 1 through 5 of 5 returned.

1. Document ID: US 20020193328 A1

L6: Entry 1 of 5 File: PGPB Dec 19, 2002

PGPUB-DOCUMENT-NUMBER: 20020193328
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020193328 A1

TITLE: Use of gene product of adenovirus early region 4 ORF-6 to inhibit repair of double-strand breaks in DNA

PUBLICATION-DATE: December 19, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Ketner, Gary	Columbia	MD	US	

US-CL-CURRENT: 514/44; 424/93.2, 435/235.1, 435/456

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. Desc | Image

2. Document ID: US 20020127714 A1

L6: Entry 2 of 5 File: PGPB Sep 12, 2002

PGPUB-DOCUMENT-NUMBER: 20020127714
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020127714 A1

TITLE: Inhibitors of alternative alleles of genes encoding products that mediate cell response to environmental changes

PUBLICATION-DATE: September 12, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Housman, David E.	Newton	MA	US	
Ledley, Fred D.	Needham	MA	US	
Stanton, Vincent P. JR.	Belmont	MA	US	

US-CL-CURRENT: 435/344; 536/23.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. Desc | Image

3. Document ID: US 6200754 B1

L6: Entry 3 of 5 File: USPT Mar 13, 2001

US-PAT-NO: 6200754
DOCUMENT-IDENTIFIER: US 6200754 B1

TITLE: Inhibitors of alternative alleles of genes encoding products that mediate cell response to environmental changes

DATE-ISSUED: March 13, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Housman; David E.	Newton	MA		
Ledley; Fred D.	Needham	MA		
Stanton, Jr.; Vincent P.	Belmont	MA		

US-CL-CURRENT: 435/6; 435/375, 536/23.1, 536/24.5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. Desc | Image

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4. Document ID: DE 69813193 E GB 2321702 A WO 9830903 A1 GB 2322193 A AU 9855684 A GB 2321702 B GB 2329469 B EP 965040 A1 AU 724108 B AU 729066 B US 6242175 B1 JP 2001508175 W EP 965040 B1

L6: Entry 4 of 5 File: DWPI May 15, 2003

DERWENT-ACC-NO: 1998-379674
DERWENT-WEEK: 200340
COPYRIGHT 2003 DERWENT INFORMATION LTD
TITLE: Screening for inhibitor of retrovirus and/or retrotransposon activity - comprises exposing component of Ku-associated DNA repair pathway to test compound, and determining the interaction

INVENTOR: DOWNS, J A; JACKSON, S P ; CRITCHLOW, S E

PRIORITY-DATA: 1997GB-0000574 (January 13, 1997), 1997GB-0013131 (June 20, 1997)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
DE 69813193 E	May 15, 2003		000	G01N033/50
GB 2321702 A	August 5, 1998		070	C12Q001/70
WO 9830903 A1	July 16, 1998	E	072	G01N033/50
GB 2322193 A	August 19, 1998		000	G01N033/68
AU 9855684 A	August 3, 1998		000	G01N033/50
GB 2321702 B	December 23, 1998		000	C12Q001/70
GB 2329469 B	September 22, 1999		000	G01N033/68
EP 965040 A1	December 22, 1999	E	000	G01N033/50
AU 724108 B	September 14, 2000		000	G01N033/50
AU 729066 B	January 25, 2001		000	G01N033/50
US 6242175 B1	June 5, 2001		000	C12Q001/70
JP 2001508175 W	June 19, 2001		058	G01N033/50
EP 965040 B1	April 9, 2003	E	000	G01N033/50

INT-CL (IPC): C12 N 9/12; C12 Q 1/48; C12 Q 1/70; G01 N 33/15; G01 N 33/50; G01 N 33/68

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

5. Document ID: DE 69813194 E WO 9830902 A1 GB 2322193 A AU 9855681 A GB 2329248 A GB 2329469 A GB 2329248 B GB 2329469 B GB 2322193 B EP 966683 A1 AU 724108 B JP 2001508868 W EP 966683 B1

L6: Entry 5 of 5 File: DWPI May 15, 2003

DERWENT-ACC-NO: 1998-399301
DERWENT-WEEK: 200340

TITLE: Modulation of cellular DNA repair activity - using compounds identified as modulating the interaction of XRCC4, DNA ligase IV and DNA-PKcs/Ku

INVENTOR: CRITCHLOW, S E; JACKSON, S P

PRIORITY-DATA: 1997GB-0013131 (June 20, 1997), 1997GB-0000574 (January 13, 1997)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
DE 69813194 E	May 15, 2003		000	G01N033/50
WO 9830902 A1	July 16, 1998	E	118	G01N033/50
GB 2322193 A	August 19, 1998		000	G01N033/68
AU 9855681 A	August 3, 1998		000	G01N033/50
GB 2329248 A	March 17, 1999		000	G01N033/68
GB 2329469 A	March 24, 1999		000	G01N033/68
GB 2329248 B	September 22, 1999		000	G01N033/68
GB 2329469 B	September 22, 1999		000	G01N033/68
GB 2322193 B	September 29, 1999		000	G01N033/68
EP 966683 A1	December 29, 1999	E	000	G01N033/50
AU 724108 B	September 14, 2000		000	G01N033/50
JP 2001508868 W	July 3, 2001		111	G01N033/50
EP 966683 B1	April 9, 2003	E	000	G01N033/50

INT-CL (IPC): C12 N 9/12; C12 Q 1/48; G01 N 33/15; G01 N 33/50; G01 N 33/566; G01 N 33/573; G01 N 33/68

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Drawi. Desc | Image

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Term	Documents
XRCC4	23
XRCC4S	0
DNA	150766
DNAS	22106
LIGASE	20496
LIGASES	2735
IV	562349
IVS	1875
PKCS	419
PKC	2848
(SCREEN$ AND (XRCC4 AND (DNA ADJ LIGASE ADJ IV) AND DNA ADJ PKCS AND PHOSPHORYLAT$)).USPT,PGPB,EPAB,DWPI,TDBD.	5

There are more results than shown above. Click here to view the entire set.

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FILE 'HOME' ENTERED AT 12:44:19 ON 16 SEP 2003

=> index bioscience medicine meetings
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI, BIOBUSINESS,
       BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT,
       CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE,
       DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 12:44:38 ON 16 SEP 2003

79 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s XRCC4 (s) (DNA (w) ligase IV) (s) (DNA (w) PK ) and phosphorylat?
          2   FILE BIOSIS
          1   FILE BIOTECHABS
          1   FILE BIOTECHDS
          1   FILE BIOTECHNO
          3   FILE CAPLUS
  16 FILES SEARCHED...
  29 FILES SEARCHED...
          2   FILE EMBASE
          2   FILE ESBIOBASE
          1*  FILE FEDRIP
          1   FILE LIFESCI
  45 FILES SEARCHED...
          2   FILE MEDLINE
          2   FILE SCISEARCH
          4   FILE USPATFULL
  65 FILES SEARCHED...
          1   FILE WPIDS
          1   FILE WPINDEX

  14 FILES HAVE ONE OR MORE ANSWERS,   79 FILES SEARCHED IN STNINDEX

L1   QUE XRCC4 (S) (DNA (W) LIGASE IV) (S) (DNA (W) PK ) AND PHOSPHORYLAT?

=> file hits
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         3.30       3.51

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FILE 'FEDRIP' ENTERED AT 12:48:21 ON 16 SEP 2003

=> s l1
L2             4 FILE USPATFULL
L3             3 FILE CAPLUS
L4             2 FILE BIOSIS
L5             2 FILE EMBASE
L6             2 FILE ESBIOBASE
L7             2 FILE MEDLINE
L8             2 FILE SCISEARCH
L9             1 FILE BIOTECHDS
L10            1 FILE BIOTECHNO
L11            1 FILE LIFESCI
L12            1 FILE WPIDS
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'XRCC4 (S) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'IV) (S) '
L13            1 FILE FEDRIP

TOTAL FOR ALL FILES
L14           22 L1

=> dup rem l14
DUPLICATE IS NOT AVAILABLE IN 'FEDRIP'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L14
L15             8 DUP REM L14 (14 DUPLICATES REMOVED)

=> d l15 1-8 ibib abs

L15  ANSWER 1 OF 8  USPATFULL on STN
ACCESSION NUMBER:         2003:244246  USPATFULL
TITLE:                    Mus101 and homologue thereof
INVENTOR(S):              Glover, David Moore, Great Gransdon Sandy, UNITED
                          KINGDOM
                          Yamamoto, Rochele, Providence, RI, UNITED STATES
                          Henderson, Daryl, Stony Brook, NY, UNITED STATES

                               NUMBER         KIND    DATE
                          ---------------- ------ --------
PATENT INFORMATION:       US 2003170655      A1   20030911
APPLICATION INFO.:        US 2002-168424     A1   20021113  (10)
                          WO 2000-GB4956          20001221
```

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1999-30708	19991224

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: LAHIVE & COCKFIELD, 28 STATE STREET, BOSTON, MA, 02109
NUMBER OF CLAIMS: 23
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 10 Drawing Page(s)
LINE COUNT: 3620

AB Plynucleotides encoding a novel Drosophila gene product designated mus101 and homologues thereof as well as mus101 polypeptides are provided. Polynucleotide probes derived from the nucleotide sequence of mus101 and antibodies that bind to mus101 protein are also provided as well as assays for identifying substances that regulate mus101 function.

L15 ANSWER 2 OF 8 USPATFULL on STN
ACCESSION NUMBER: 2003:237799 USPATFULL
TITLE: Electrophoretic assay to predict risk of cancer and the efficacy and toxicity of cancer therapy
INVENTOR(S): Stevens, Craig W., Houston, TX, UNITED STATES
Ismail, Sheikh, Houston, TX, UNITED STATES
Buchholz, Thomas, West University, TX, UNITED STATES
Story, Michael, Houston, TX, UNITED STATES
Brock, William, Houston, TX, UNITED STATES
PATENT ASSIGNEE(S): Board of Regents, The University of Texas System (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003165956	A1	20030904
APPLICATION INFO.:	US 2003-351247	A1	20030124 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-351732P	20020125 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FULBRIGHT & JAWORSKI L.L.P., 600 CONGRESS AVE., SUITE 2400, AUSTIN, TX, 78701
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 23 Drawing Page(s)
LINE COUNT: 1562

AB The present invention provides a method for predicting the risk of occurrence of cancer. It also predicts the presence of BRCA mutations which in turn predicts the risk of developing breast cancer in women. Further, it assesses a cancer patient's level of sensitivity to chemotherapy.

L15 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2003:52927 CAPLUS
DOCUMENT NUMBER: 138:380218
TITLE: Coordinated Assembly of Ku and p460 Subunits of the DNA-dependent Protein Kinase on DNA Ends is Necessary for XRCC4-ligase IV Recruitment
AUTHOR(S): Calsou, Patrick; Delteil, Christine; Frit, Philippe; Drouet, Jerome; Salles, Bernard
CORPORATE SOURCE: CNRS UMR 5089, Institut de Pharmacologie et de Biologie Structurale, Toulouse, 31077, Fr.
SOURCE: Journal of Molecular Biology (2003), 326(1), 93-103
CODEN: JMOBAK; ISSN: 0022-2836

PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Repair of DNA double-strand breaks by the non-homologous end-joining pathway (NHEJ) requires a minimal set of proteins including DNA-dependent protein kinase (**DNA-PK**), **DNA-ligase IV** and **XRCC4** proteins. DNA-PK comprises Ku70/Ku80 heterodimer and the kinase subunit DNA-PKcs (p460). Here, by monitoring protein assembly from human nuclear cell exts. on DNA ends in vitro, we report that recruitment to DNA ends of the XRCC4-ligase IV complex responsible for the key ligation step is strictly dependent on the assembly of both the Ku and p460 components of DNA-PK to these ends. Based on co-immunopptn. expts., we conclude that interactions of Ku and p460 with components of the XRCC4-ligase IV complex are mainly DNA-dependent. In addn., under p460 kinase permissive conditions, XRCC4 is detected at DNA ends in a **phosphorylated** form. This **phosphorylation** is DNA-PK-dependent. However, **phosphorylation** is dispensable for XRCC4-ligase IV loading to DNA ends since stable DNA-PK/XRCC4-ligase IV/DNA complexes are recovered in the presence of the kinase inhibitor wortmannin. These findings extend the current knowledge of the assembly of NHEJ repair proteins on DNA termini and substantiate the hypothesis of a scaffolding role of DNA-PK towards other components of the NHEJ DNA repair process.
REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 8 USPATFULL on STN
ACCESSION NUMBER: 2002:235524 USPATFULL
TITLE: Inhibitors of alternative alleles of genes encoding products that mediate cell response to environmental changes
INVENTOR(S): Housman, David E., Newton, MA, UNITED STATES
Ledley, Fred D., Needham, MA, UNITED STATES
Stanton, Vincent P., JR., Belmont, MA, UNITED STATES
PATENT ASSIGNEE(S): Variagenics, Inc., a Delaware corporation (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002127714	A1	20020912
APPLICATION INFO.:	US 2001-782837	A1	20010214 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1998-45054, filed on 19 Mar 1998, PATENTED
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: ANITA L. MEIKLEJOHN, PH.D., FISH & RICHARDSON P.C., 225 Franklin Street, Boston, MA, 02110-2804
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Page(s)
LINE COUNT: 3790
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are methods for the treatment of proliferative disorders using compounds and/or environmental conditions which result in a difference in sensitivity of targeted and non-targeted cells. Certain of the methods involve the identification and use of allele-specific inhibitors of conditionally essential genes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2003:16313 CAPLUS
DOCUMENT NUMBER: 138:165640
TITLE: The DNA-Dependent Protein Kinase Interacts with DNA To Form a Protein-DNA Complex That Is Disrupted by

Phosphorylation

AUTHOR(S): Merkle, Dennis; Douglas, Pauline; Moorhead, Greg B. G.; Leonenko, Zoya; Yu, Yaping; Cramb, David; Bazett-Jones, David P.; Lees-Miller, Susan P.
CORPORATE SOURCE: Department of Biochemistry Molecular Biology, University of Calgary, Calgary, AB, T2N 4N1, Can.
SOURCE: Biochemistry (2002), 41(42), 12706-12714
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB DNA double-strand breaks are a serious threat to genome stability and cell viability. One of the major pathways for the repair of DNA double-strand breaks in human cells is nonhomologous end-joining. Biochem. and genetic studies have shown that the DNA-dependent protein kinase (**DNA-PK**), **XRCC4**, **DNA ligase IV**, and Artemis are essential components of the nonhomologous end-joining pathway. DNA-PK is composed of a large catalytic subunit, DNA-PKcs, and a heterodimer of Ku70 and Ku80 subunits. Current models predict that the Ku heterodimer binds to ends of double-stranded DNA, then recruits DNA-PKcs to form the active protein kinase complex. XRCC4 and DNA ligase IV are subsequently required for ligation of the DNA ends. Magnesium-ATP and the protein kinase activity of DNA-PKcs are essential for DNA double-strand break repair. However, little is known about the physiol. targets of DNA-PK. We have previously shown that DNA-PKcs and Ku undergo autophosphorylation, and that this correlates with loss of protein kinase activity. Here we show, using electron spectroscopic imaging, that DNA-PKcs and Ku interact with multiple DNA mols. to form large protein-DNA complexes that converge at the base of multiple DNA loops. The no. of large protein complexes and the amt. of DNA assocd. with them were dramatically reduced under conditions that promote **phosphorylation** of DNA-PK. Moreover, treatment of autophosphorylated DNA-PK with the protein phosphatase 1 catalytic subunit restored complex formation. We propose that autophosphorylation of DNA-PK plays an important regulatory role in DNA double-strand break repair by regulating the assembly and disassembly of the DNA-PK-DNA complex.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 8 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2002-06020 BIOTECHDS
TITLE: Stimulating non-homologous end-joining of DNA for treating cancer or retroviral infections, comprises performing end-joining of DNA in the presence of inositol hexakisphosphate or other stimulatory inositol phosphate; vector-mediated DNA-dependent protein-kinase or DNA-ligase gene transfer and expression in host cell for gene therapy
AUTHOR: WEST S C; HANAKAHI L A A; BARTLET-JONES M
PATENT ASSIGNEE: IMPERIAL CANCER RES TECHNOLOGY LTD
PATENT INFO: WO 2001090404 29 Nov 2001
APPLICATION INFO: WO 2000-GB2180 20 May 2000
PRIORITY INFO: US 2001-268367 14 Feb 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-075375 [10]
AN 2002-06020 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - Stimulating (M) non-homologous end-joining (NHEJ) of DNA, comprises performing NHEJ of DNA in the presence of inositol hexakisphosphate (IP6) or another stimulatory inositol phosphate (SIP).
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an assay of NHEJ of DNA comprising IP6 or another SIP; (2) use of IP6 or other SIP for stimulating NHEJ of DNA; (3) a kit of parts comprising IP6 or other SIP and one or more of a DNA-dependent protein kinase (PK), **XRCC4**, **DNA ligase IV**

, or a host cell expressing the protein and a suitable DNA substrate; (4) an assay of a PK or for NHEJ of DNA which comprises IP6 or other SIP; (5) a kit of parts comprising a PK, or a host cell expressing PK, and IP6 or other SIP; (6) identifying a compound which modulates or mimics the effect of IP6 or other SIP in stimulating NHEJ of DNA, by: (a) performing NHEJ of DNA in the presence of the IP6 or other SIP and determining the effect of a test compound on the NHEJ of DNA; or (b) determining in the presence of IP6 or other SIP, the effect of a test compound on the interactions between the components of NHEJ reaction mixture; (7) identifying a compound which modulates the NHEJ of DNA, by determining the effect of an inositol phosphate or its derivative on NHEJ of DNA; (8) identifying a compound which modulates or mimics the effect of IP6 or other SIP on PK, by determining in the presence of IP6 or other SIP, the effect of a test compound on the catalytic activity of PK or on the ability of PK to interact with another component; (9) identifying a compound which modulates the binding of IP6 or other SIP to a PK, **XRCC4** or **DNA ligase IV**, by determining whether a test compound reduces or increases the binding of IP6 or other SIP to PK or its subunit, **XRCC4** or **DNA ligase IV**; (10) a compound identifiable or identified by the above methods (6)-(8); (11) reducing NHEJ of DNA comprising reducing the amount of, or inhibiting the stimulatory effect of IP6 or other SIP in a NHEJ reaction; (12) enhancing NHEJ of DNA comprising increasing the amount of or enhancing or mimicking the stimulatory effect of IP6 or other SIP in an NHEJ reaction; (13) modulating the activity or interaction of PK by changing the amount of IP6 or other SIP present with PK, or inhibiting or enhancing the effect of IP6 or other SIP on PK; and (14) determining whether an individual has or is predisposed to a defect in DNA repair or cell cycle checkpoint control, by obtaining a sample from the patient, determining the concentration of, or subcellular localization of, IP6 or other SIP in the sample, and comparing the result with a standard.

BIOTECHNOLOGY - Preferred Method: IP6 or other SIP is exogenous IP6 or other SIP. The NHEJ of DNA is performed in vitro in a NHEJ reaction mixture which includes DNA-dependent PK (or a component such as Ku 70/80 heterodimer or its subunit), **XRCC4**, **DNA ligase IV**, a suitable DNA substrate, ATP and Mg2+. PK has a domain with similarity to the catalytic domain of phosphatidylinositol 3-kinase and is chosen from: (i) DNA-dependent PK, ATR, ATM, FRAP; (ii) Saccharomyces cerevisiae gene products Tel1p, Mec1p, Tor1p or Tor2p; or (iii) Schizosaccharomyces pombe gene product Rad3. In method (8), the effect of a test compound on the interaction between the catalytic subunit of a DNA-dependent PK and any one of Ku70, Ku80, **DNA ligase IV**, **XRCC4** or its suitable DNA substrate is determined. In method (9), the subunit is the Ku70/80 heterodimer of **DNA-PK** or the Ku70 or Ku80 subunit. The test compound is an inositol derivative, a phosphoinositide or an analog of IP6 or another SIP and a compound which mimics or modulates the effect of IP6 or other SIP is selected for further study. Preferred Kit: One or more of DNA dependent PK, **XRCC4** and **DNA ligase IV** are expressed from a recombinant nucleic acid molecule. PK is expressed from a recombinant nucleic acid and the kit further comprises a substrate for PK.

ACTIVITY - Cytostatic; virucide; vasotropic; anti-HIV; immunomodulatory;

MECHANISM OF ACTION - Gene therapy regimens improver; NHEJ of DNA modulator; protein kinase modulator. The stimulation of DNA-protein kinase (PK) dependent NHEJ by inositol phosphate was studied. Commercially available IP6 was assayed for its ability to stimulate end-joining by a cell extract which contained all components required for NHEJ in vivo (Ku70/80, DNA-PKcs, **XRCC4** and **DNA ligase IV**). IP6 stimulated end-joining at concentrations in the region of 100 nM and stimulation was maximal at 1 micro Molar. To assess the specificity of NHEJ for IP6, the ability of IP6 to stimulate end-joining with other inositol phosphates (IP5, IP4 and

IP3) was compared. In addition, inositol hexasulfate (IS6), an inositol compound which provides a charge distribution similar to that of IP6, while presenting sulfate rather than phosphate groups was also assayed. It was found that IS6 was unable to stimulate end-joining, demonstrating a clear requirement for phosphate groups. IP6 proved to be the most effective inositol phosphate compound of those tested. IP5 and IP4 were also able to stimulate end-joining, but the efficiency of this stimulation was reduced relative to IP6. The data showed that end-joining required a **phosphorylated** inositol species, and the stimulation of NHEJ was directly related to the extend of **phosphorylation**.

USE - (M) is useful for modulating NHEJ of DNA in a human or animal cell in need of reduction or enhancement in NHEJ of DNA and for treating cancer, augmenting cancer radiotherapy and/or chemotherapy regimes, improving gene therapy regimes, enhancing homologous recombination, treating retroviral infections, or modulating the immune system and to treat patients who are immunocompromized or susceptible to cancer due to impaired checkpoint cell cycle control. Compounds which may be useful in developing agents for treating the above conditions may be identified. Agents may be developed for modulating PK activity or interactions and for identifying compounds which modulate cell cycle checkpoint control (all claimed). Modulators of ATM or ATR are useful for treating ataxia-telangiectasia, acquired immunodeficiency syndrome (AIDS) and other conditions, modulating the immune system, telomere length and augmenting cancer and radiotherapy or chemotherapy.

ADMINISTRATION - Administered by oral or parenteral, e.g. subcutaneous or intramuscular routes. No dosage is specified. (104 pages)

L15 ANSWER 7 OF 8 USPATFULL on STN

ACCESSION NUMBER:	2001:36603 USPATFULL
TITLE:	Inhibitors of alternative alleles of genes encoding products that mediate cell response to environmental changes
INVENTOR(S):	Housman, David E., Newton, MA, United States Ledley, Fred D., Needham, MA, United States Stanton, Jr., Vincent P., Belmont, MA, United States
PATENT ASSIGNEE(S):	Variagenics, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6200754	B1	20010313	
APPLICATION INFO.:	US 1998-45054		19980319	(9)
DOCUMENT TYPE:	Utility			
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PRIMARY EXAMINER:	Schwartzman, Robert A.			
ASSISTANT EXAMINER:	Epps, Janet L.			
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NUMBER OF DRAWINGS:	3 Drawing Figure(s); 3 Drawing Page(s)			
LINE COUNT:	3654			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are methods for the treatment of proliferative disorders using compounds and/or environmental conditions which result in a difference in sensitivity of targeted and non-targeted cells. Certain of the methods involve the identification and use of allele-specific inhibitors of conditionally essential genes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 8 OF 8 FEDRIP COPYRIGHT 2003 NTIS on STN

ACCESSION NUMBER:	2003:141994 FEDRIP
NUMBER OF REPORT:	CRISP 2R01AI48758-04
RESEARCH TITLE:	Relevant Targets of the DNA Dependent Protein Kinase
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SAFETY&TOXICOLOGY BLDG
PERFORMING ORGN: MICHIGAN STATE UNIVERSITY, EAST LANSING, MICHIGAN
SUPPORTING ORGN: Supported By: NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
PROJECT START DATE: 2003 (/15/00)
FISCAL YEAR: 2003
ESTD COMPLETION DATE: 2002 (/28/08)
FUNDING: Competing Continuation (Type 2)
FILE SEGMENT: National Institutes of Health

SUM DESCRIPTION (provided by applicant): Efficient repair of DNA double strand breaks is essential for the maintenance of chromosomal integrity and persistence of higher organisms. In higher eukaryotes, non-homologous DNA end joining (NHEJ) is the primary pathway that repairs these breaks. NHEJ also functions in developing lymphocytes to repair strand breaks that occur during VDJ recombination, the site-specific recombination process that provides for assembly of functional antigen receptor genes. If VDJ recombination is impaired, B and T lymphocyte development is blocked resulting in the disease, severe combined immunodeficiency [SCID]. In the last decade, an intensive research effort has focused on NHEJ resulting in a reasonable understanding of how DSBs are resolved. Six distinct gene products have been identified which function in this pathway [Ku70, Ku86, **XRCC4**, **DNA ligase IV**, Artemis, and DNA-PKcs]. Three of these comprise one complex, the DNA dependent protein kinase (**DNA-PK**). This protein complex is central during non-homologous end joining because **DNA-PK** initially recognizes and binds to damaged DNA and then targets other repair activities to the site of DNA damage. Though recent data demonstrate unequivocally that **DNA-PK**'s kinase activity is essential during NHEJ, it is not clear why. That **DNA-PK** alters the function of one or more important mediator(s) of NHEJ is the central hypothesis to be tested in the proposed studies. Five of the six factors known to function in NHEJ are targets of **DNA-PK**'s kinase activity (either in vitro or in vivo); only **DNA ligase IV** is not. However, to date there is no compelling evidence that **phosphorylation** of any of these factors is functionally relevant. The proposed research will map **DNA-PK**'s target **phosphorylation** sites in each of these five factors. Using a mutational approach, we will then determine whether **DNA-PK phosphorylation** of each factor is functionally relevant. In sum, since the non-homologous end-joining pathway is critical for the maintenance of genomic integrity, understanding how this pathway functions is of unquestionable relevance. However, our understanding of how nonhomologous DNA end joining works will be incomplete without a clear understanding of what factor(s) are activated by **DNA-PK**'s kinase activity.

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